monitoring the fluorescence of the [flurophore] fluorophore, the generation of fluorescence corresponding to the occurrence of nucleic acid amplification.

(Amended) 2. The method of claim 1 wherein the amplification is carried out using [nucleic acid polymerase is] a thermostable nucleic acid polymerase.

(Amended) 3. The method of claim 1 wherein the fluorophore on the first probe and the quencher molecule on the second probe are on complementary [the same hybridized] base pairs.

REMARKS

The Examiner has rejected claims 1-11 in paragraphs 9 a-b and 9 d-f and claim 2 in paragraph 9 c and claim 3 in paragraph 9 g under 35 U.S.C. 112, second paragraph. The Applicants have amended the claims in response to each of paragraphs 9 a-g. Applicants believe that the amendments have traversed the Section 112, paragraph 2 rejection.

The Examiner has rejected claims 1-11 under 35 USC 102(e) as allegedly anticipated by Di Cesare 5,716,784. DiCesare does not teach nor does it suggest the claimed invention. Di Cesare teaches that an "analytical probe" containing a 5' fluorophore anneals to a target sequence during the extension portion of a PCR reaction. The analytical probe is blocked at its 3' end and cannot be extended and is then hydrolyzed by use of an enzyme, i.e., a nucleic acid polymerase, having 5' to 3' exonuclease activity. This enzyme thereby liberates individual nucleotides or dinucleotides, some of which contain the 5' fluorophore. This liberation of the 5'fluorophore individual nucleotides or dinucleotides provides the basis for the measurement of the degree of amplification of target that has occurred. The claimed invention does not require the use of a polymerase having 5' to 3' exonuclease activity. Claim 1 has been amended to clarify this aspect of the invention. Rather, the claimed invention relies on the binding of the entire fluorescently labeled probe to a target sequence and accordingly the disassociation of the probes from each

other in proportion to the amount of amplification which has occurred, thereby resulting in a proportionate decrease in the quenching of the fluorophore probe by the otherwise adjacent quencher probe. In this regard, the Examiner's attention is drawn to both Morrison references cited in the Information Disclosure Statement submitted herewith. Neither Morrison reference teaches or suggests the use of a shorter and a longer probe that assists in favoring hybridization of the probe to the target over rehybridization of the probes to each other. Nor does Di Cesare alone or in combination with either Morrison reference (any suggestion to so combine not being acceded to by Applicants) teach such an advantageous use of differing probe lengths.

Applicants respectfully submit that the Examiner's rejections have been traversed and that the prior claims and the newly added claims are presently in condition for allowance. The Examiner may contact the undersigned at the phone number set forth below, should she feel it helpful to further the prosecution of this application.

Respectfully submitted,

9/17/99
Date

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